#4

OIPE

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/910,186A

DATE: 11/28/2001 TIME: 13:08:12

Input Set : A:\09910186seqlist.txt

Output Set: N:\CRF3\11212001\I910186A.raw



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1 <110> APPLICANT: U.S. Army Medical Research & Material Command
      4 <120> TITLE OF INVENTION: RECOMBINANT VACCINE AGAINST BOTULINUM
              NEUROTOXIN
      7 <130> FILE REFERENCE: A33626-A 067252.0107
C--> 9 <140> CURRENT APPLICATION NUMBER: US/09/910,186A
C--> 9 <141> CURRENT FILING DATE: 2001-07-20
      9 <150> PRIOR APPLICATION NUMBER: PCT/US00/12890
     10 <151> PRIOR FILING DATE: 2000-05-12
     12 <150> PRIOR APPLICATION NUMBER: 09/611,419
     13 <151> PRIOR FILING DATE: 2000-07-06
     15 <150> PRIOR APPLICATION NUMBER: 60/133,865
     16 <151> PRIOR FILING DATE: 1999-05-12
     18 <150> PRIOR APPLICATION NUMBER: 60/133,866
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     21 <150> PRIOR APPLICATION NUMBER: 60/133,867
     22 <151> PRIOR FILING DATE: 1999-05-12
     24 <150> PRIOR APPLICATION NUMBER: 60/133,868
     25 <151> PRIOR FILING DATE: 1999-05-12
     27 <150> PRIOR APPLICATION NUMBER: 60/133,869
     28 <151> PRIOR FILING DATE: 1999-05-12
     30 <150> PRIOR APPLICATION NUMBER: 60/133,873
     31 <151> PRIOR FILING DATE: 1999-05-12
     33 <150> PRIOR APPLICATION NUMBER: 08/123,975
     34 <151> PRIOR FILING DATE: 1993-09-21
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     38 <170> SOFTWARE: FastSEQ for Windows Version 4.0
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    41 <211> LENGTH: 1332
    42 <212> TYPE: DNA
    43 <213> ORGANISM: Artificial Sequence
    45 <220> FEATURE:
    46 <223> OTHER INFORMATION: Synthetic construct based on Clostridium botulinum
    47
              sequence
    49 <221> NAME/KEY: CDS
    50 <222> LOCATION: (13)...(1326)
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    55
                     Met Arg Leu Leu Ser Thr Phe Thr Glu Tyr Ile Lys Asn
    58 atc atc aat acc tcc atc ctg aac ctg cgc tac gaa tcc aat cac ctg
    59 Ile Ile Asn Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu
            15
                                 20
    62 atc gac ctg tct cgc tac gct tcc aaa atc aac atc ggt tct aaa gtt
    63 Ile Asp Leu Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val
    66 aac ttc gat ccg atc gac aag aat cag atc cag ctg ttc aat ctg gaa
                                                                           195
    67 Asn Phe Asp Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu
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Input Set : A:\09910186seqlist.txt
Output Set: N:\CRF3\11212001\1910186A.raw

68					50					55					60		
	tct	tcc	aaa	atc		qtt	atc	ctq	aaq		qct	atc	qta	tac		tct	243
					-	_		_	-		-	Ile	_				
72			-	65					70					75			
74	atg	tac	gaa	aac	ttc	tcc	acc	tcc	ttc	tgg	atc	cgt	atc	ccg	aaa	tac	291
75	Met	Tyr	Glu	Asn	Phe	Ser	Thr	Ser	Phe	Trp	Ile	Arg	Ile	Pro	Lys	Tyr	
76			80					85					90				
78	ttc	aac	tcc	atc	tct	ctg	aac	aat	gaa	tac	acc	atc	atc	aac	tgc	atg	339
79	Phe	Asn	Ser	Ile	Ser	Leu	Asn	Asn	Glu	Tyr	Thr	Ile	Ile	Asn	Cys	Met	
80		95					100					105					
	-							-		_		tac		_			387
		Asn	Asn	Ser	Gly	\mathtt{Trp}	Lys	Val	Ser	Leu	Asn	Tyr	Gly	Glu	Ile	Ile	
-	110					115					120					125	
			_	_	-		_	_			_	cgt	-	-			435
	Trp	Thr	Leu	Gln		Thr	Gln	Glu	Ile		Gln	Arg	Val	Val		Lys	
88					130					135					140		
			_	_					_			aat	_				483
	Tyr	Ser	GIn		шe	Asn	TTE	Ser	_	Tyr	He	Asn	Arg	_	ITe	Phe	
92				145		4_			150					155			F 0.4
												aaa					531
	Val	THE	160	THE	ASII	ASII	Arg	165	ASII	ASII	ser	Lys	170	туг	тте	ASII	
96	~~~	00+		2+0	~~~	~~~	222		a + a	+	~ ~ +	a+ a			-+-		F70
		-	-		-	_		_				ctg Leu					579
100	_	175		116	изр	GIII	180		116	261	ASII	185	_	ASII	TTE	птъ	
				. aac	ato	ato			cta	. σac	aat			. uac	act	cac	627
	-					_			_	-		_	_	_		His	027
	190		11.51	1 11011		195			, LCu	. mop	200	_	1119	,	, 1111	205	
			ato	taa	ato			tto	aat	cta			aaa	ι σα α	cto	aac	675
												-		_	_	Asn	
108		_		-	210		-			215			4		220		
110	gaa	aaa	gaa	ato	aaa	gac	ctg	tac	gac	aac	cag	r tcc	aat	tct	ggt	atc	723
																, Ile	
112				225					230					235	;		
114	ctg	aaa	gac	ttc	tgg	ggt	gac	tac	ctg	cag	tac	gac	aaa	ccg	tac	tac	771
115	Leu	Lys	Asp	Phe	Trp	Gly	Asp	Tyr	Leu	Gln	Туг	: Asp	Lys	Pro	Tyr	Tyr	
116			240					245					250				
	-	_		_		_	_				_	_	_			gta	819
	Met			Leu	Tyr	Asp			Lys	Tyr	· Val	. Asp	Val	. Asn	Asn	Val	
120		255					260			, ,		265					
																atg	867
			Arg	Gly	Tyr			Leu	Lys	GTA		_	Gly	Ser	· Val	Met	
	270					275					280					285	015
																ttc	915
	Thr	Thr	ASI	тте			Asn	ser	ser			arg	GTÄ	Thr		Phe	
128	2+-	+-			290		+~+	~~+		295			- - -		300		063
																aac	963
132	116	тте	туу	тув 305		HIG	ser	стХ		_	ASP	ASN	тте		_	Asn	
132				303					310					315			

RAW SEQUENCE LISTING DATE: 11/28/2001 PATENT APPLICATION: US/09/910,186A TIME: 13:08:12

Input Set : A:\09910186seqlist.txt

Output Set: N:\CRF3\11212001\I910186A.raw

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134 aat gat cgt gta tac atc aat gtt gta gtt aag aac aaa gaa tac cgt
                                                                       1011
135 Asn Asp Arg Val Tyr Ile Asn Val Val Lys Asn Lys Glu Tyr Arg
            320
                                 325
                                                     330
138 ctg gct acc aat gct tct cag gct ggt gta gaa aag atc ttg tct gct
                                                                       1059
139 Leu Ala Thr Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala
                            340
142 ctg gaa atc ccg gac gtt ggt aat ctg tct cag gta gtt gta atg aaa
                                                                       1107
143 Leu Glu Ile Pro Asp Val Gly Asn Leu Ser Gln Val Val Wat Lys
                        355
                                             360
146 tcc aag aac gac cag ggt atc act aac aaa tgc aaa atg aat ctg cag
                                                                       1155
147 Ser Lys Asn Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln
                    370
                                         375
150 gac aac aat ggt aac gat atc ggt ttc atc ggt ttc cac cag ttc aac
                                                                       1203
151 Asp Asn Asn Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn
152
                385
                                    390
154 aat atc gct aaa ctg gtt gct tcc aac tgg tac aat cgt cag atc gaa
                                                                       1251
155 Asn Ile Ala Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu
            400
                                405
                                                     410
158 cgt tcc tct cgc act ctg ggt tgc tct tgg gag ttc atc ccg gtt gat
                                                                       1299
159 Arg Ser Ser Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp
        415
                          420
                                                 425
162 gac ggt tgg ggt gaa cgt ccg ctg taa gaattc
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163 Asp Gly Trp Gly Glu Arg Pro Leu *
164 430
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168 <211> LENGTH: 437
169 <212> TYPE: PRT
170 <213> ORGANISM: Artificial Sequence
172 <220> FEATURE:
173 <223> OTHER INFORMATION: Synthetic construct based on Clostridium botulinum
          sequence
177 <400> SEQUENCE: 2
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180 Thr Ser Ile Leu Asn Leu Arg Tyr Glu Ser Asn His Leu Ile Asp Leu
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182 Ser Arg Tyr Ala Ser Lys Ile Asn Ile Gly Ser Lys Val Asn Phe Asp
184 Pro Ile Asp Lys Asn Gln Ile Gln Leu Phe Asn Leu Glu Ser Ser Lys
                            55
                                                 60
186/ Ile Glu Val Ile Leu Lys. Asn Ala Ile Val Tyr Asn Ser Met Tyr Glu
                                             75
188 Asn Phe Ser Thr Ser Phe Trp Ile Arg Ile Pro Lys Tyr Phe Asn Ser
190 Ile Ser Leu Asn Asn Glu Tyr Thr Ile Ile Asn Cys Met Glu Asn Asn
191
                100
                                    105
                                                         110
192 Ser Gly Trp Lys Val Ser Leu Asn Tyr Gly Glu Ile Ile Trp Thr Leu
            115
                                120
194 Gln Asp Thr Gln Glu Ile Lys Gln Arg Val Val Phe Lys Tyr Ser Gln
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Output Set: N:\CRF3\11212001\1910186A.raw

```
130
                             135
196 Met Ile Asn Ile Ser Asp Tyr Ile Asn Arg Trp Ile Phe Val Thr Ile
                        150
                                             155
198 Thr Asn Asn Arg Leu Asn Asn Ser Lys Ile Tyr Ile Asn Gly Arg Leu
                    165
                                         170
200 Ile Asp Gln Lys Pro Ile Ser Asn Leu Gly Asn Ile His Ala Ser Asn
                                     185
                180
202 Asn Ile Met Phe Lys Leu Asp Gly Cys Arg Asp Thr His Arg Tyr Ile
            195
                                 200
                                                     205
204 Trp Ile Lys Tyr Phe Asn Leu Phe Asp Lys Glu Leu Asn Glu Lys Glu
                             215
206 Ile Lys Asp Leu Tyr Asp Asn Gln Ser Asn Ser Gly Ile Leu Lys Asp
                                             235
208 Phe Trp Gly Asp Tyr Leu Gln Tyr Asp Lys Pro Tyr Tyr Met Leu Asn
209
210 Leu Tyr Asp Pro Asn Lys Tyr Val Asp Val Asn Asn Val Gly Ile Arg
211
                                     265
212 Gly Tyr Met Tyr Leu Lys Gly Pro Arg Gly Ser Val Met Thr Thr Asn
214 Ile Tyr Leu Asn Ser Ser Leu Tyr Arg Gly Thr Lys Phe Ile Ile Lys
                            295
                                                 300
216 Lys Tyr Ala Ser Gly Asn Lys Asp Asn Ile Val Arg Asn Asn Asp Arg
                        310
                                             315
218 Val Tyr Ile Asn Val Val Lys Asn Lys Glu Tyr Arg Leu Ala Thr
                    325
                                         330
220 Asn Ala Ser Gln Ala Gly Val Glu Lys Ile Leu Ser Ala Leu Glu Ile
                                     345
222 Pro Asp Val Gly Asn Leu Ser Gln Val Val Wat Lys Ser Lys Asn
            355
                                360
224 Asp Gln Gly Ile Thr Asn Lys Cys Lys Met Asn Leu Gln Asp Asn Asn
                            375
                                                 380
226 Gly Asn Asp Ile Gly Phe Ile Gly Phe His Gln Phe Asn Asn Ile Ala
                        390
228 Lys Leu Val Ala Ser Asn Trp Tyr Asn Arg Gln Ile Glu Arg Ser Ser
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230 Arg Thr Leu Gly Cys Ser Trp Glu Phe Ile Pro Val Asp Asp Gly Trp
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                                    425
232 Gly Glu Arg Pro Leu
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236 <210> SEQ ID NO: 3
237 <211> LENGTH: 1323
238 <212> TYPE: DNA
239 <213> ORGANISM: Artificial Sequence
241 <220> FEATURE:
242 <223> OTHER INFORMATION: Synthetic construct based on Clostridium botulinum
243
          sequence
246 <221> NAME/KEY: CDS
247 <222> LOCATION: (13)...(1314)
248 <223> OTHER INFORMATION: Synthetic Construct
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DATE: 11/28/2001 PATENT APPLICATION: US/09/910,186A TIME: 13:08:12

Input Set : A:\09910186seqlist.txt

Output Set: N:\CRF3\11212001\1910186A.raw

	gaa		EQUE aaa	cg a	tg t											tc aa [.] le Ası	
253					1				5		-			10			
255	acc	tcc	atc	ctg	aac	ctg	cgc	tac	gaa	tcc	aat	cac	ctq	atc	gac	cta	99
256	Thr	Ser	Ile	Leu	Asn	Leu	Arg	Tyr	Ğlu	Ser	Asn	His	Leu	Ile	Asp	Leu	
257		15					20	-				25					
259	tct	cgc	tac	gct	tcc	aaa	atc	aac	atc	aat	tct	aaa	att	aac	ttc	αat	147
260	Ser	Arg	Tyr	Āla	Ser	Lys	Ile	Asn	Ile	Glv	Ser	Lvs	Val	Asn	Phe	Asp	
261			•			35				1	40	-10			1110	45	
263	ccq	atc	gac	aaq	aat	cag	atc	caσ	cta	t.t.c	aat	cta	αаа	tet	tcc		195
264	Pro	Ile	Āsp	Lys	Asn	Gln	Ile	Gln	Leu	Phe	Asn	Leu	Glu	Ser	Ser	Lvs	100
265			-	•	50		_			55			0		60	275	
267	atc	qaa	qtt	atc	ctq	aaq	aat	act	atc		tac	aac	tet	atα	tac	gaa	243
268	Ile	Ğlu	val	Ile	Leu	Lvs	Asn	Ala	Ile	Val	Tvr	Asn	Ser	Met	Tyr	Glu	243
269				65					70		-1-		,	75	-1-	Olu	
271	aac	ttc	tcc	acc	tcc	ttc	taa	atc	cat	atc	cca	aaa	tac		aac	tcc	291
272	Asn	Phe	Ser	Thr	Ser	Phe	Trp	Ile	Ara	Tle	Pro	Lvs	Tyr	Phe	Asn	Ser	2,71
273			80					85	,			-1-	90			DCI	
275	atc	tct	ctq	aac	aat	gaa	tac		atc	atc	aac	tac		αаа	aac	aat	339
276	Ile	Ser	Leu	Asn	Asn	Ğlu	Tvr	Thr	Ile	Ile	Asn	Cvs	Met	Glu	Asn	Asn	333
277		95					100					105		a			
279	tct	aat	taa	aaa	gta	tct		aac	tac	aat	αаа		atc	taa	act	cta	387
280	Ser	ĞÎy	Trp	Lvs	Val	Ser	Leu	Asn	Tvr	Glv	Glu	Tle	Tle	Trn	Thr	Leu	307
	110	4	•			115			-1-	- 1	120				1111	125	
283	caq	qac	act	caq	qaa		aaa	caσ	cat	at.t.		ttc	aaa	tac	tct		435
284	Gln	Asp	Thr	Gln	Ğlu	Ile	Lvs	Gln	Ara	Val	Val	Phe	Lvs	Tvr	Ser	Gln	133
285		-			130		-1-		9	135				- 1 -	140	0111	
287	atg	atc	aac	atc	tct	qac	tac	atc	aat		t.aa	atc	ttc	at.t.	acc	atc	483
288	Met	Ile	Asn	Ile	Ser	Asp	Tyr	Ile	Asn	Ara	Trp	Ile	Phe	Val	Thr	Tle	100
289				145		-	- 4		150	5	r			155		110	
291	acc	aac	aat	cqt	ctq	aat	aac	tcc		atc	tac	atc	aac		cgt	cta	531
292	Thr	Asn	Asn	Arg	Leu	Asn	Asn	Ser	Lvs	Ile	Tvr	Ile	Asn	Glv	Arg	Len	331
293			160	_				165			-1-		170	1	9	Lou	
295	atc	gaç	cag	aaa	ccq	atc	tcc	aat	cta	aat	aac	atc		act.	tct	aat	579
															Ser		3,3
297		175		-			180			- 4		185					
299	aac	atc	atg	ttc	aaa	ctq	qac	aat	tat	cat	gac		cac	cac	tac	atc	627
300	Asn	Ile	Met	Phe	Lys	Leu	Asp	Gly	Cvs	Ara	Asp	Thr	His	Ara	Tyr	Tle	02,
301	190				-	195	_	- 1	- 4		200			5	-1-	205	
		atc	aaa	tac	ttc	aat	ctq	ttc	gac	aaa		cta	aac	σaa	aaa		675
304	Trp	Ile	Lys	Tyr	Phe	Asn	Leu	Phe	Asp	Lvs	Glu	Leu	Asn	Glu	Lys	Glu	0,5
305	-		-	-	210					215					220		
307	atc	aaa	gac	ctg	tac	gac	aac	caq	tcc		tct	aat	atc	cta	aaa	gac	723
308	Ile	Lys	Āsp	Leu	Tyr	Asp	Asn	Gln	Ser	Asn	Ser	Glv	Ile	Leu	Lys	Asp	, 20
309		-	-	225	-	-			230			r		235	-10		
	ttc	tgg	ggt	gac	tac	ctg	cag	tac		aaa	cca	tac	tac		ctg	aat	771
312	Phe	Trp	Gly	Āsp	Tyr	Leu	Gln	Tyr	Asp	Lys	Pro	Tyr	Tyr	Met	Leu	Asn	
313		_	240	-	-			245	-	-		-	250				

VERIFICATION SUMMARY

DATE: 11/28/2001 PATENT APPLICATION: US/09/910,186A TIME: 13:08:13

Input Set : A:\09910186seqlist.txt
Output Set: N:\CRF3\11212001\I910186A.raw

L:9 M:270 C: Current Application Number differs, Replaced Current Application No L:9 M:271 C: Current Filing Date differs, Replaced Current Filing Date